Extensive Extranodal Involvement of Rare Sites in Non Hodgkin's Lymphoma Detected on ^{18}F - FDG PET-CT: A Case Report

Varun Singh Dhull · Punit Sharma · Suhas Singla ·
Nauroze Asghar Faizi · Sanjay Thulkar ·
Chandersekhar Bal · Rakesh Kumar

Received: 11 July 2012 / Revised: 16 October 2012 / Accepted: 23 October 2012 / Published online: 9 November 2012
© Korean Society of Nuclear Medicine 2012

Abstract We present a case of a 23 year-old male treated for Hodgkin's lymphoma who developed diffuse large B-cell lymphoma (DLBCL) 8 years after achieving remission. ^{18}F -fluorodeoxyglucose positron emission tomography computed tomography (^{18}F -FDG PET-CT) was done, which revealed extensive extranodal involvement of bilateral atria, bilateral kidneys, ileo-caecal junction and left testis along with mesenteric and retroperitoneal lymph nodal involvement. Renal and cardiac lesions were not detected by contrast-enhanced CT. Simultaneous lymphomatous involvement of rare sites such as heart, kidneys and testis in a single patient has not been reported before.

Keywords Extranodal · Non Hodgkin's lymphoma · Atria · Kidneys · Testis · ^{18}F -FDG · PET-CT

Introduction

Lymphoma is composed of indolent as well as aggressive human malignancies which arise from cells of the immune system at different stages of differentiation. They can

manifest in a wide range of morphologic, immunologic and clinical findings. Malignancies of lymphoid cells may present as leukemia (i.e., primary involvement of bone marrow and blood), or as lymphoma (i.e., solid tumors of the immune system) [1]. The role of ^{18}F -fluorodeoxyglucose positron emission tomography (^{18}F -FDG PET) and PET-CT (positron emission tomography-computed tomography) has been extensively evaluated in the management of Hodgkin's disease (HD) and non Hodgkin's lymphoma (NHL) [2–7]. PET-CT has shown significant improvement in staging and restaging when compared to conventional imaging modalities such as contrast-enhanced computed tomography (CECT) [4–7]. The role of ^{18}F -FDG PET-CT in detection, staging and restaging of patients with extranodal involvement in NHL has also been reported in the literature [2, 3]. Multiple isolated cases with extranodal involvement of NHL, detected on PET-CT, have been previously reported [8–11]. Here, we report a rare case of extranodal NHL involving multiple organs namely heart, bilateral kidneys, bowel, and left testis, in addition to mesenteric and retroperitoneal lymph nodes which were detected on ^{18}F -FDG PET-CT.

Case Report

We report a case of a 23 year-old male who was treated for Hodgkin's lymphoma of cervical lymph nodes (Stage IA) in 2003. He was in remission until 2011, when he developed intermittent, mild epigastric abdominal pain. He was prescribed a 2-week course of proton pump inhibitors and the symptoms apparently improved but recurred. Two weeks later, the abdominal pain intensified and became more generalized, along with constitutional symptoms like fever and lethargy. There were no cardiac symptoms. Abdominal

V. S. Dhull · P. Sharma · S. Singla · N. A. Faizi · C. Bal ·
R. Kumar (✉)
Department of Nuclear Medicine,
All India Institute of Medical Sciences,
Ansari Nagar,
New Delhi 110029, India
e-mail: rkphulia@hotmail.com

R. Kumar
e-mail: rkphulia@yahoo.com

N. A. Faizi · S. Thulkar
Department of Radiodiagnosis,
All India Institute of Medical Sciences,
New Delhi, India

Fig. 1 Transaxial thorax CECT image (a) didn't reveal any focal cardiac lesion. Transaxial abdominal CECT images did not show any renal lesion (b). It revealed presence of enlarged left testis (c), circumferential soft tissue attenuation thickening of the terminal ileum (arrow)

more pronounced along the medial wall with adjacent small ileo-caecal node (d) and well margined soft tissue attenuation lesions in left para-aortic (arrow) (e) and precaval location (arrow) (f) consistent with lymphomatous ileal involvement and nodal deposits

examination revealed slightly distended abdomen, decreased bowel sounds and diffuse tenderness, most prominent in the right lower quadrant. Cardiovascular examination was unremarkable. The pulse was 88/min, regular, blood pressure was 118/78 mm of Hg and jugular venous pressure was not elevated. The heart sounds were audible and normal and there was no murmur, heave or rub. CECT of the abdomen and thorax revealed asymmetric thickening of the terminal ileum, along with multiple mesenteric and retroperitoneal lymphadenopathy (Fig. 1). Colonoscopy revealed ileo-colic intussusception and biopsy results of the lesion were consistent with diffuse large B-cell lymphoma (DLBCL). Serum lactate dehydrogenase levels were elevated (630 IU/L). The patient was thereafter referred to the nuclear medicine department for staging ^{18}F -FDG PET-CT. PET-CT showed abnormally increased ^{18}F -FDG uptake in right and left atria, bilateral renal cortices, left testis, terminal ileum, ileo-caecal junction, and in multiple mesenteric and retroperitoneal lymph nodes (Figs. 2 and 3). Renal and cardiac lesions were not detected on CECT. Maximum standardized uptake value (SUV_{max}) and size of various nodal and extranodal lesions are given in the Table 1. The patient underwent equilibrium radionuclide gated blood-pool angiography (ERNA) for ejection fraction estimation prior to chemotherapy. It showed an ejection fraction of 60 % (normal >50 %) and no ventricular wall motion abnormality. The patient underwent combination chemotherapy with cyclophosphamide, hydroxydaunorubicin, oncovin and prednisone along with rituximab (R-CHOP regimen). ^{18}F -FDG PET-CT was repeated after four cycles of chemotherapy

to assess treatment response. It showed progression of disease at all sites including heart, kidneys and testes (Fig. 4). Interestingly secondary to bilateral testicular involvement, the

Fig. 2 Maximum intensity projection images of PET-CT scan shows multifocal increased ^{18}F -FDG uptake in the mediastinum (arrow head), gastrointestinal tract (outline arrow and connected arrow), kidneys (thin black arrow) and scrotal region (thick black arrow)

Fig. 3 Transaxial PET-CT images show focally increased ^{18}F -FDG uptake in bilateral atria (a) and bilateral renal cortices (b). It also shows a left testicular mass with intense ^{18}F -FDG uptake (c), ileo-cecal mass with intense ^{18}F -FDG uptake (d), ^{18}F -FDG avid retroperitoneal (e) and mesenteric (f) lymphadenopathy. Findings were suggestive of lymphomatous involvement of above mentioned sites

patient developed bilateral testicular vein thrombosis. The patient is now being planned for second line chemotherapy.

Discussion

Patients treated for HD are infrequently known to develop NHL; it is not clear whether it is due to the dedifferentiation of existing disease or due to secondary effects of its treatment [1]. The involvement of extranodal sites is a common feature in the course of NHL. Moreover, some NHLs are considered to originate at sites other than the lymph nodes or the spleen, and are referred to as primary extranodal NHL (PE-NHL) [12, 13]. When NHL has extranodal presence, the involved sites can be the gastrointestinal tract, bone, brain, testis, ovary, lung, nasopharynx, soft tissue, thyroid, kidney, liver, breast, skin, etc. [14, 15].

DLBCL is the most common type of NHL, constituting 33 % of all cases. The patient can present either with a primary disease of lymph nodes or that of extranodal sites. More than half of the patients have some site of extranodal involvement at the time of initial diagnosis. Any organ can be involved, with the most common sites being the gastrointestinal tract and bone marrow, each being involved in 15–20 % of the patients [1]. Extranodal involvement in DLBCL is associated with a decreased overall survival rate in Stage I DLBCL. Paradoxically, a better outcome is observed in DLBCL stage IV patients with concomitant extranodal disease [16].

Gastrointestinal tract is involved in 10–30 % of all patients with NHL. The stomach is the most commonly affected followed by small bowel, large bowel, and esophagus [2]. In the small bowel, NHL usually occurs due to the direct extension of disease from the involved mesenteric lymph nodes and the distal ileum is most frequently affected

site [17]. In the present case, mesenteric lymph nodes along with the distal ileum were involved, which culminated in the ileo-colic intussusception.

Testicular lymphoma, whether primary or secondary to the extensive disease, is a rare entity. The most common histological type is DLBCL. Inguinal and retroperitoneal lymph nodal spread can also be seen in some patients [2]. In our case, there was abnormally increased asymmetric radiotracer uptake in the enlarged left testis. Also, multiple retroperitoneal (para-aortic and pre-aortic) lymph nodes showed abnormal ^{18}F -FDG accumulation, signifying likely lymphomatous spread from the involved testis. Yin et al. reported a case of a 55-year-old man with NHL of the left testis and of the bilateral adrenals detected by ^{18}F -FDG PET-CT and demonstrated its role in the diagnosis and assessment of therapeutic response [8].

Renal involvement is quite uncommon in DLBCL. In most of the cases it is secondary and occurs by hematogenous spread or by direct extension of the disease from a retroperitoneal mass. Villa et al. concluded that there is a high incidence of central nervous system relapse in patients with DLBCL and kidney involvement at diagnosis [18–20].

Table 1 Describing SUVmax and dimension of lesions detected in PET/CT

Site of involvement	SUV _{max}	Size (cms)
Ileum	24.5	8.7
Mesenteric lymph nodes	22.7	3.6
Retroperitoneal lymph nodes	17.1	2.8
Left and right renal cortices	4.2, 13.9	0.5, 1.7
Left and right atria	15.8, 12.6	2.2, 1.7
Left testis	21.9	6.4

Fig. 4 Images of ^{18}F -FDG PET-CT done after four cycles of chemotherapy. Maximum intensity projection images of PET-CT scan (**a**) shows multifocal increased ^{18}F -FDG uptake in the mediastinum (*arrow head*), gastrointestinal tract (*line arrow and connected arrow*), kidneys (*non solid black arrow*) and bilateral testes (*solid black arrow*). As compared to baseline PET-CT there is progression of disease at all sites including heart (**b**), kidneys (**c**) and testes (**d**). Interestingly, there is linear increased ^{18}F -FDG uptake in bilateral testicular veins due to thrombosis (**a**, *broken arrows*)

As ^{18}F -FDG is excreted by the kidneys, it can lead to false positive and false negative interpretations on PET-CT. Renal involvement in NHL is seen as multiple focal areas of increased ^{18}F -FDG uptake mostly in renal cortices that may be unilateral or less commonly, bilateral. There may or may not be corresponding lesions in non diagnostic CT scans [2]. In the present case, multiple focal areas of increased radiotracer uptake were noted in bilateral renal cortices. These lesions were isodense and non-enhancing on CECT.

Heart and pericardium are rarely involved in NHL. The involvement is usually revealed by cardiac complications and is associated with a poor prognosis [21, 22]. Few cases of cardiac involvement in NHL have been reported, both primary and metastatic, detected by ^{18}F -FDG PET-CT [9–11]. Julian et al. reported two cases of NHL with cardiac involvement (apical septum, right ventricle and right auricle) detected by ^{18}F -FDG PET-CT that allowed an early diagnosis and chemotherapy, therefore, improving the survival [9]. Synchronous lesions were detected in bilateral atria in our case, which were isodense and non-enhancing on CECT and therefore missed on CT.

Therefore, whole body imaging with a sensitive modality such as ^{18}F -FDG PET-CT is mandatory to assess the extent of disease by detecting unexpected extranodal sites of disease or exclusion of disease in the presence of nonspecific extranodal CT findings [3]. In patients with known disease, other goals can be accomplished,

which are evaluation of response to therapy (progression was demonstrated in the present case), identification of new or recurrent disease, and monitoring the complications of therapy. In patients, where the disease has not been confirmed, imaging helps in reaching a provisional diagnosis [23].

In conclusion, the present case highlights the utility of ^{18}F -FDG PET-CT in detection of extranodal NHL at unsuspected sites which may have an important bearing on the management and prognosis.

References

1. Armitage JO, Longo DL. Malignancies of lymphoid cells. In: Kasper DL, Braunwald E, Fauci AS, et al., editors. (15): Harrison's principles of Internal Medicine. New York: The McGraw-Hill Companies; 2005. p. 641–55.
2. Paes FM, Kalkanis DG, Sideras PA, Serafini AN. FDG PET/CT of Extranodal Involvement in Non-Hodgkin Lymphoma and Hodgkin Disease. *RadioGraphics*. 2010;30:269–91.
3. Even-Sapir E, Lievshitz G, Perry C, Herishanu Y, Lerman H, Metser U. Fluorine-18 Fluorodeoxyglucose PET/CT Patterns of Extranodal Involvement in Patients with Non-Hodgkin Lymphoma and Hodgkin's Disease. *Radiol Clin N Am*. 2007;45:697–709.
4. Pelosi E, Pregno P, Penna D, Deandreis D, Chiappella A, Limerutti G, et al. Role of whole-body [18F] fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) and conventional techniques in the staging of patients with Hodgkin

- and aggressive non Hodgkin lymphoma. *Radiol Med*. 2008;113:578–90.
5. Kumar R, Maillard I, Schuster SJ, Alavi A. Utility of fluorodeoxyglucose-PET imaging in the management of patients with Hodgkin's and non-Hodgkin's lymphomas. *Radiol Clin North Am*. 2004;42:1083–100.
 6. Jerusalem G, Bequin Y, Fassotte MF, Najjar F, Paulus P, Rigo P, et al. Whole-body positron emission tomography using 18F-fluorodeoxyglucose for posttreatment evaluation in Hodgkin's disease and non-Hodgkin's lymphoma has higher diagnostic and prognostic value than classical computed tomography scan imaging. *Blood*. 1999;15:429–33.
 7. Specht L. 2-[18F]fluoro-2-deoxyglucose positron-emission tomography in staging, response evaluation, and treatment planning of lymphomas. *Semin Radiat Oncol*. 2007;17:190–7.
 8. Yin Y, Qing F, Li X, Du B, Li N, Li Y. Non Hodgkin's lymphoma of the testicle and bilateral adrenals detected by 18F-FDG PET/CT. *Exp Theor Med*. 2011;2:817–20.
 9. Julian A, Wagner T, Ysebaert L, Chabbert V, Payoux P. FDG PET/CT leads to the detection of metastatic involvement of the heart in non-Hodgkin's lymphoma. *Eur J Nucl Med Mol Imaging*. 2011;38:1174.
 10. Kaderli AA, Baran I, Aydin O, Bicer M, Akpinar T, Ozkalemkas F, et al. Diffuse involvement of the heart and great vessels in primary cardiac lymphoma. *Eur J Echocardiogr*. 2010;11:74–6.
 11. Su HY, Huang HL, Sun CM, Hou SM, Chen ML. Primary cardiac lymphoma evaluated with integration of PET/CT and contrast-enhanced CT. *Clin Nucl Med*. 2009;34:298–301.
 12. d'Amore F, Christensen BE, Brincker H, Pedersen NT, Thorling K, Hastrup J, et al. features and prognostic factors in extranodal non-Hodgkin lymphomas. Danish LYFO Study Group. *Eur J Cancer*. 1991;27:1201–8.
 13. Economopoulos T, Asprou N, Stathakis N, Papageorgiou E, Dervenoulas J, Xanthaki K, et al. Primary extranodal non-Hodgkin's lymphoma in adults: clinicopathological and survival characteristics. *Leuk Lymphoma*. 1996;21:131–6.
 14. Lopez-Guillermo A, Colomo L, Jimenez M, Bosch F, Villamor N, Arenillas L, et al. Diffuse large B-cell lymphoma: clinical and biological characterization and outcome according to the nodal or extranodal primary origin. *J Clin Oncol*. 2005;23:2797–804.
 15. Economopoulos T, Papageorgiou S, Rontogianni D, Kaloutsi V, Fountzilas G, Tsatalas C, et al. Multifocal Extranodal Non-Hodgkin Lymphoma: α clinicopathologic study of 37 Cases in Greece, a Hellenic Cooperative Oncology Group Study. *Oncologist*. 2005;10:734–8.
 16. Moller MB, Pedersen NT, Christensen BE. Diffuse large B-cell lymphoma: clinical implications of extranodal versus nodal presentation—a population-based study of 1575 cases. *Br J Haematol*. 2004;124:151–9.
 17. Levine MS, Rubesin SE, Pantongrag-Brown L, Buck JL, Herlinger H, et al. Non-Hodgkin's lymphoma of the gastrointestinal tract: radiographic findings. *AJR Am J Roentgenol*. 1997;168:165–72.
 18. Heiken JP, Gold RP, Schnur MJ, King DL, Bashist B, Glazer HS. Computed tomography of renal lymphoma with ultrasound correlation. *J Comput Assist Tomogr*. 1983;7:245–50.
 19. Sheth S, Ali S, Fishman E. Imaging of renal lymphoma: patterns of disease with pathologic correlation. *RadioGraphics*. 2006;26:1151–68.
 20. Villa D, Connors JM, Sehn LH, Gascoyne RD, Savage KJ. Diffuse large B-cell lymphoma with involvement of the kidney: outcome and risk of central nervous system relapse. *Haematologica*. 2011;96:1002.
 21. Guermazi A, Brice P, de Kerviler EE, Fermé C, Hennequin C, Meignin V, et al. Extranodal Hodgkin disease: spectrum of disease. *RadioGraphics*. 2011;21:161–79.
 22. van den Bos EJ, Baks T, Bakker J, van Gelder W, Levin MD. Severe right ventricular inflow obstruction by non-Hodgkin lymphoma. *Br J Haematol*. 2008;142:858.
 23. Leite NP, Kased N, Hanna RF, Brown MA, Pereira JM, Cunha R, et al. Cross-sectional Imaging of Extranodal Involvement in Abdominopelvic Lymphoproliferative Malignancies. *RadioGraphics*. 2007;27:1613–34.